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| Applicant's or agent's file reference<br>35561 WOP00 JFO/ltn   | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416). |  |
| International Application No.<br><b>PCT/AU2003/000746</b>  | International Filing Date<br>(day/month/year)<br>13 June 2003  | Priority Date (day/month/year)<br>13 June 2002 |
| International Patent Classification (IPC) or national classification and IPC<br><b>Int. Cl. <sup>7</sup> C12N 15/10; C12Q 1/68</b> |  |  |
| Applicant<br><b>NUCLEICS PTY LTD et al</b>   |  |  |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

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|---|--|
| Date of submission of the demand<br>18 December 2003  | Date of completion of the report<br>22 September 2004                              |
| Name and mailing address of the IPEA/AU<br>AUSTRALIAN PATENT OFFICE<br>PO BOX 200, WODEN ACT 2606, AUSTRALIA<br>E-mail address: pct@ipaaustralia.gov.au<br>Facsimile No. (02) 6285 3929 | Authorized Officer<br><br><b>CHRISTOPHER LUTON</b><br>Telephone No. (02) 6283 2256 |

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☒ the international application as originally filed.
- ☐ the description,      pages      , as originally filed,  
                                 pages      , filed with the demand,  
                                 pages      , received on      with the letter of
- ☐ the claims,      pages      , as originally filed,  
                                 pages      , as amended (together with any statement) under Article 19,  
                                 pages      , filed with the demand,  
                                 pages      , received on      with the letter of
- ☐ the drawings,      pages      , as originally filed,  
                                 pages      , filed with the demand,  
                                 pages      , received on      with the letter of
- ☐ the sequence listing part of the description:  
                                 pages      , as originally filed  
                                 pages      , filed with the demand  
                                 pages      , received on      with the letter of

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

**4. ☐ The amendments have resulted in the cancellation of:**

- ☐ the description,      pages
- ☐ the claims,      Nos.
- ☐ the drawings,      sheets/fig.

**5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be nonobvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos: 1-4 and 8-36 (all partially)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claim Nos. 1-4 and 8-36 (all partially) – see supplemental box.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.  
☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

|                               |             |     |
|-------------------------------|-------------|-----|
| Novelty (N)                   | Claims 1-36 | YES |
|                               | Claims      | NO  |
| Inventive step (IS)           | Claims 1-36 | YES |
|                               | Claims      | NO  |
| Industrial applicability (IA) | Claims 1-36 | YES |
|                               | Claims      | NO  |

**2. Citations and explanations (Rule 70.7)**

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1 - Electrophoresis, 2001, vol. 22, no. 2, Katsura et al.

D2 - Chemical Abstracts, abstract accession no. 138:67155

The present invention relates to methods for performing certain chemical reactions wherein the methods involve the 'collapse' of an emulsion. In the emulsions, reactants are initially maintained within the discontinuous phase. Upon collapse of the emulsion, the reactant(s) become part of the continuous phase whereupon a chemical reaction may take place. The incorporation of reactants within the discontinuous phase of emulsions also offers the advantage that submicrolitre-scale reactions may be performed using microlitre-scale liquid handling equipment.

**NOVELTY (N) and INVENTIVE STEP (IS)**

D1 discloses the incorporation of very small amounts of reactants within the droplets of an emulsified aqueous phase. D1 expressly suggests the fusion of 'microreactors' having different reactants (bottom of first column). The emulsions of D1 would address the problem of manipulation of minute amounts of reactants. However, D1 does not disclose 'collapse' of the emulsions such that the reactants are mixed as part of the continuous phase of the emulsion. Therefore, the claims are novel and involve an inventive step in light of the D1.

D2 alludes to the use of water-in-oil emulsions in PCR as a means of handling small-scale sample volumes. D2 suggests collapse of the emulsion by "using the water phase sepd. From the emulsion". An English language translation of the abstracted article was not available to this office. However, Figure 4 of the abstracted article appears to suggest formation of a continuous phase from the previously discontinuous phase. However, the abstract does not expressly disclose or suggest collapse of emulsion to effect a reaction between the reactants. Therefore, the claims appear to be novel and inventive in light of D2.

**VI. Certain documents cited****1. Certain published documents (Rule 70.10)**

| Application No.<br>Patent No. | Publication date<br>(day/month/year) | Filing date<br>(day/month/year) | Priority date ( valid claim)<br>(day/month/year) |
|-------------------------------|--------------------------------------|---------------------------------|--|
| JP 2003-153692                | 27 May 2003                          | 25 March 2002                   | 7 September 2001                                 |
| WO 2002/103011                | 27 December 2002                     | 18 June 2002                    | 18 June 2001                                     |

JP 2003-153692 discloses nucleic-acid amplification reactions conducted in emulsions and collection of the discontinuous phase as a continuous phase. WO 2002/103011 discloses nucleic acid replication within an emulsion (page 34, line 4-page 36, line 31). WO 2002/103011 also discloses formation of a continuous phase from the discontinuous phase (page 37 lines 23-26). If the priority of the present application is found to be invalid these documents may become relevant to an assessment of the novelty or inventive step of the claims.

**2. Non-written disclosures (Rule 70.9)**

| Kind of non-written disclosure | Date of non-written disclosure<br>(day/month/year) | Date of written disclosure referring to<br>non-written disclosure<br>(day/month/year) |
|--------------------------------|--|---|
|--------------------------------|--|---|

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

**Continuation of Box III**

As noted in the International Search Report, claims 1-4 and 8-36 (all partially) do not define the matter for which protection is sought in terms of the technical features of the invention (Rule 6.3(a)).

The independent claims 1, 4, 34, 35 and 36 broadly encompass any chemical reaction involving the 'collapse' of an emulsion wherein a reactant is found in one or other phase of the emulsion. *Prima facie*, the claims therefore encompass, *inter alia*, well known chemical techniques such as 'emulsion polymerisation'\*.

The specification, when read as a whole, indicates that the invention relates to the use of the described methods in nucleic acid sequencing and amplification reactions. The specification only exemplifies reactions involving the amplification of sequencing of nucleic acids. Therefore, the claims have been searched and examined only to the extent that they are limited to reactions involving sequencing, amplification or other manipulations of nucleic acids.

\* Polymer Science Dictionary, Alger, Elsevier Applied Science, 1989.